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PASSWORD:
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 NEWS  1           Web Page for STN Seminar Schedule - N. America
 NEWS  2  NOV 21   CAS patent coverage to include exemplified prophetic
                   substances identified in English-, French-, German-,
                   and Japanese-language basic patents from 2004-present
 NEWS  3  NOV 26   MARPAT enhanced with FSORT command
 NEWS  4  NOV 26   CHEMSAFE now available on STN Easy
 NEWS  5  NOV 26   Two new SET commands increase convenience of STN
                   searching
 NEWS  6  DEC 01   ChemPort single article sales feature unavailable
 NEWS  7  DEC 12   GBFULL now offers single source for full-text
                   coverage of complete UK patent families
 NEWS  8  DEC 17   Fifty-one pharmaceutical ingredients added to PS
 NEWS  9  JAN 06   The retention policy for unread STNmail messages
                   will change in 2009 for STN-Columbus and STN-Tokyo
 NEWS 10  JAN 07   WPIDS, WPINDEX, and WPIX enhanced Japanese Patent
                   Classification Data
 NEWS 11  FEB 02   Simultaneous left and right truncation (SLART) added
                   for CERAB, COMPUAB, ELCOM, and SOLIDSTATE
 NEWS 12  FEB 02   GENBANK enhanced with SET PLURALS and SET SPELLING
 NEWS 13  FEB 06   Patent sequence location (PSL) data added to USGENE
 NEWS 14  FEB 10   COMPENDEX reloaded and enhanced
 NEWS 15  FEB 11   WTEXTILES reloaded and enhanced
 NEWS 16  FEB 19   New patent-examiner citations in 300,000 CA/CAplus
                   patent records provide insights into related prior
                   art
 NEWS 17  FEB 19   Increase the precision of your patent queries -- use
                   terms from the IPC Thesaurus, Version 2009.01
 NEWS 18  FEB 23   Several formats for image display and print options
                   discontinued in USPATFULL and USPAT2
 NEWS 19  FEB 23   MEDLINE now offers more precise author group fields
                   and 2009 MeSH terms
 NEWS 20  FEB 23   TOXCENTER updates mirror those of MEDLINE - more
                   precise author group fields and 2009 MeSH terms
 NEWS 21  FEB 23   Three million new patent records blast AEROSPACE into
                   STN patent clusters
 NEWS 22  FEB 25   USGENE enhanced with patent family and legal status
                   display data from INPADOCDB
 NEWS 23  MAR 06   INPADOCDB and INPAFAMDB enhanced with new display
                   formats

 NEWS EXPRESS JUNE 27 08 CURRENT WINDOWS VERSION IS V8.3,
              AND CURRENT DISCOVER FILE IS DATED 23 JUNE 2008.
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 NEWS IPC8      For general information regarding STN implementation of IPC 8

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FILE 'HOME' ENTERED AT 12:57:19 ON 06 MAR 2009

=> file reg
COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                         0.22       0.22

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STRUCTURE FILE UPDATES:     4 MAR 2009  HIGHEST RN 1115640-24-8
DICTIONARY FILE UPDATES:    4 MAR 2009  HIGHEST RN 1115640-24-8

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http://www.cas.org/support/stngen/stndoc/properties.html

=>
Uploading C:\Program Files\STNEXP\Queries\10599918 I to III.str
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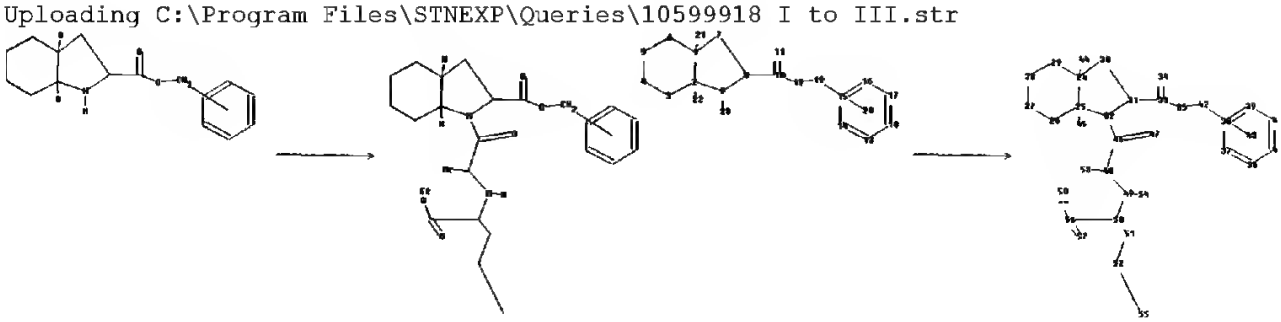

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chain nodes :
10  11  12  19  21  22  23  33  34  35  42  44  45  46  47  48  49  50  51  52  53
54  55  56  57  58  59
ring nodes :
1  2  3  4  5  6  7  8  9  13  14  15  16  17  18  24  25  26  27  28  29  30  31
32  36  37  38  39  40  41
chain bonds :
1-21  2-22  8-10  9-23  10-11  10-12  12-19  24-44  25-45  31-33  32-46  33-34  33-
35
35-42  46-47  46-48  48-49  48-53  49-50  49-54  50-51  50-56  51-52  52-55  56-57
56-58  58-59

ring bonds :
1-2  1-6  1-7  2-3  2-9  3-4  4-5  5-6  7-8  8-9  13-14  13-18  14-15  15-16  16-17
17-18  24-25  24-29  24-30  25-26  25-32  26-27  27-28  28-29  30-31  31-32  36-37
36-41  37-38
38-39  39-40  40-41
exact/norm bonds :
2-9  8-9  10-11  10-12  25-32  31-32  32-46  33-34  33-35  46-47  48-49  49-50  56-
57
56-58
exact bonds :
1-2  1-6  1-7  1-21  2-3  2-22  3-4  4-5  5-6  7-8  8-10  9-23  12-19  24-25  24-29
24-30  24-44  25-26  25-45  26-27  27-28  28-29  30-31  31-33  35-42  46-48  48-53
49-54  50-51
50-56  51-52  52-55  58-59
normalized bonds :
13-14  13-18  14-15  15-16  16-17  17-18  36-37  36-41  37-38  38-39  39-40  40-41

isolated ring systems :
containing 1 : 24 :


Match level :
1:Atom  2:Atom  3:Atom  4:Atom  5:Atom  6:Atom  7:Atom  8:Atom  9:Atom  10:CLASS
11:CLASS  12:CLASS  13:Atom  14:Atom  15:Atom  16:Atom  17:Atom  18:Atom  19:CLASS
20:Atom  21:CLASS
22:CLASS  23:CLASS  24:Atom  25:Atom  26:Atom  27:Atom  28:Atom  29:Atom  30:Atom
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51:CLASS  52:CLASS
53:CLASS  54:CLASS  55:CLASS  56:CLASS  57:CLASS  58:CLASS  59:CLASS
fragments assigned product role:
containing 24
fragments assigned reactant/reagent role:
containing 1



L1      STRUCTURE UPLOADED

=> d l1
L1 HAS NO ANSWERS
L1              STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY -  AVAILABLE VIA OFFLINE PRINT *
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Structure attributes must be viewed using STN Express query preparation.

=> file casreact
COST IN U.S. DOLLARS | SINCE FILE ENTRY | TOTAL SESSION
FULL ESTIMATED COST | 0.48 | 0.70

FILE 'CASREACT' ENTERED AT 12:57:54 ON 06 MAR 2009
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FILE CONTENT:1840 - 2 Mar 2009 VOL 150 ISS 10

New CAS Information Use Policies, enter HELP USAGETERMS for details.

****
*
* CASREACT now has more than 16.5 million reactions *
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=> s l1 SSS full
FULL SEARCH INITIATED 12:57:58 FILE 'CASREACT'
SCREENING COMPLETE - 165 REACTIONS TO VERIFY FROM 26 DOCUMENTS

100.0% DONE 165 VERIFIED 39 HIT RXNS 15 DOCS
SEARCH TIME: 00.00.01

L2 15 SEA SSS FUL L1 (39 REACTIONS)

=> d ibib abs fhit 1-
YOU HAVE REQUESTED DATA FROM 15 ANSWERS - CONTINUE? Y/(N):y

L2 ANSWER 1 OF 15 CASREACT COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 149:386408 CASREACT Full-text
TITLE: Process for the preparation of perindopril erbumine salt and novel polymorph (s) thereof
INVENTOR(S): Desai, Parimal Hansmukh; Salvi, Narenda Jagannath; Patravale, Bharatkumar Surendra; Subramanian, Seetharaman; Kajale, Nitin Baburao; Dabe, Avikumar Digamber

PATENT ASSIGNEE(S): Aarti Healthcare Limited, India
SOURCE: PCT Int. Appl., 26pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2008114270	A1	20080925	WO 2007-IN120	20070322

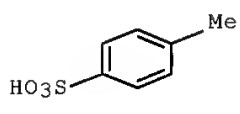
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

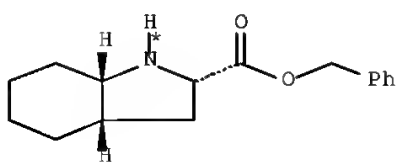
PRIORITY APPLN. INFO.: WO 2007-IN120 20070322

AB This invention relates to single pot process for the preparation of perindopril erbumine salt according to which condensation of (2S, 3aS, 7aS)-octahydroindole-2-carboxylic acid benzyl ester para toluene sulfonate with N-((S-)-ethoxy carbonyl -1-ethyl-(S)-alanine) catalytic hydrogenation of benzyl ester of (2S, 3aS, 7aS)-1-{2-[1-(ethoxycarbonyl)-(S)-butylamino]-(S)propionyl}- octahydro-indole-2-carboxylate and conversion of (2S,3aS, 7aS)-1-{2-[1-(ethoxycarbonyl)-(S)-butylamino]-(S)- propionyl}octahydroindole-2-carboxylic acid to its perindopril erbumine salt are carried out in a single pot using a single solvent such as iso-Pr acetate to obtain perindopril erbumine salt of very high purity. Also a novel polymorph S of perindopril erbumine having X-ray diffraction peaks of 9.10, 14.64, 15.37, 16.58, 17.39, 19.99, 20.62, 21.50, 22.15, 22.60, 24.20, 27.55 ± 0.2 at 2Θ values. Also processes for preparing the novel polymorph S.

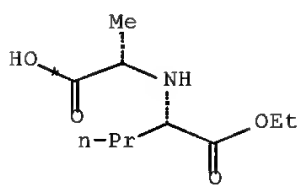
RX(1) OF 6 A + B ===> C...



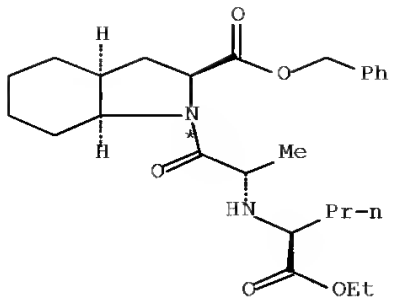
A: CM 1



A: CM 2



B

(1) 

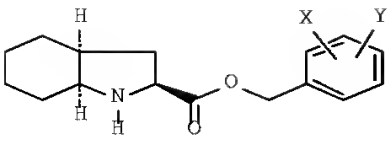
C

RX(1) RCT A 94062-52-9, B 82834-12-6
PRO C 122454-52-8
SOL 108-21-4 Acetic acid, 1-methylethyl ester, 121-44-8 Et3N, 2592-95-2 1-Benzotriazolol, 25952-53-8 EDAP
CON SUBSTAGE(1) 25 - 30 deg C
SUBSTAGE(2) 5 - 10 deg C
REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 2 OF 15 CASREACT COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 148:55381 CASREACT Full-text
TITLE: Process for the preparation of perindopril and intermediates thereof
INVENTOR(S): Haider, Akhtar; Megevand, Sophie; Nicollier, Brigitte; Pannatier, Yvan
PATENT ASSIGNEE(S): Sochinaz SA, Switz.
SOURCE: Eur. Pat. Appl., 19pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1864973	A1	20071212	EP 2006-11981	20060609
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, YU				

PRIORITY APPLN. INFO.: EP 2006-11981 20060609
OTHER SOURCE(S): MARPAT 148:55381
GI



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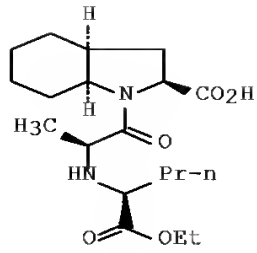
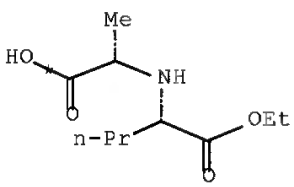


III

AB The invention provides a novel method for the synthesis of (2S,3αS,7αS)-octahydroindole-2-carboxylic acid (I) and its aryl esters II [wherein X, Y = H, halo, alkyl, alkoxyl or nitro group], and the conversion of the p-nitrobenzyl ester of the acid into perindopril or its salts. II were obtained via esterification of racemic octahydroindole-2-carboxylic acid hydrochloride with benzyl alcs. in the presence of aryl sulfonic acids such as p-TsOH, followed by resolution with such as dibenzoyl-(L)-tartaric acid. Alternatively, II could be synthesized directly by esterification of chiral I with benzyl alcs. For example, I was reacted with p-nitrobenzyl alc. in the presence of p-TsOH to afford p-tosylate salt of the corresponding ester in 79% yield, which underwent DCC/HOBt-mediated coupling reaction with N-[(S)-1-(ethoxycarbonyl)butyl]-(S)-alanine in dichloromethane (80% yield). Pd/C-catalyzed hydrogenolysis of the resultant p-nitrobenzyl ester led to perindopril.

RX(5) OF 21 ...R + Q ===> S...



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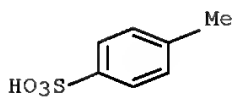
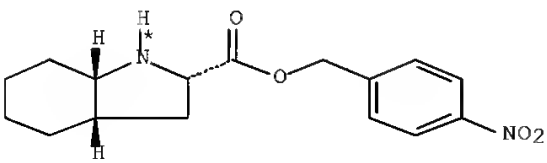


Q: CM 1



Q: CM 2

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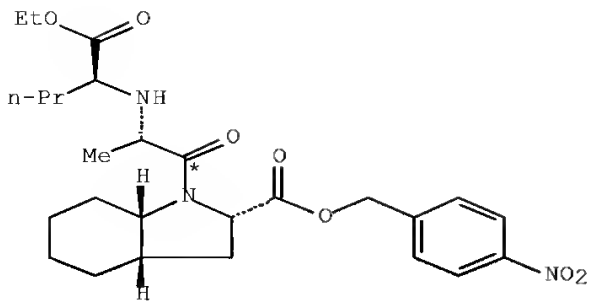

S
YIELD 80%

RX(5) RCT R 82834-12-6

STAGE(1)
SOL 75-09-2 CH2C12
CON 10 minutes, room temperature

STAGE(2)
RCT Q 959984-64-6
RGT T 121-44-8 Et3N, U 2592-95-2 1-Benzotriazolol
SOL 75-09-2 CH2C12
CON SUBSTAGE(1) room temperature
SUBSTAGE(2) 15 minutes, room temperature

STAGE(3)
RGT V 538-75-0 DCC
CON SUBSTAGE(1) room temperature -> 5 deg C
SUBSTAGE(3) 5 hours, room temperature
SUBSTAGE(4) 1 hour, room temperature -> 5 deg C

PRO S 866430-96-8
NTE workup
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 3 OF 15 CASREACT COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 147:212285 CASREACT Full-text
TITLE: Process for the preparation of N-[1-(S)-ethoxycarbonyl-1-butyl]-(s)-alanine-DMT complex and its use in the preparation of perindopril
INVENTOR(S): Joshi, Narendra Shriram; Pradhan, Nitin Sharad Chandra
PATENT ASSIGNEE(S): Glenmark Pharmaceuticals Limited, India
SOURCE: PCT Int. Appl., 16pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2007085933	A2	20070802	WO 2007-IB150	20070123

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: IN 2006-MU125 20060125
US 2006-792875P 20060418

OTHER SOURCE(S): MARPAT 147:212285

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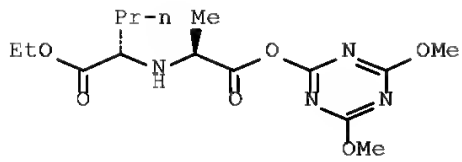

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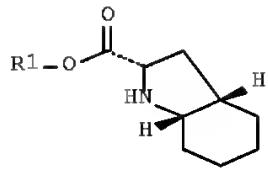
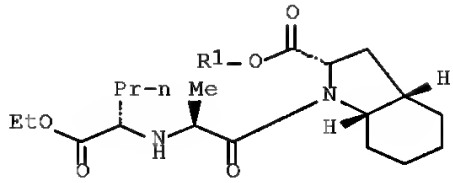


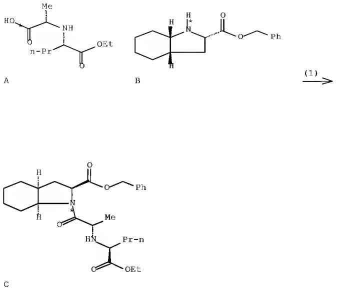
II



III

AB A process for the preparation of N-[1-(S)-ethoxycarbonyl-1-butyl]-L-alanine-DMT complex (I) by reaction of N-[1-(S)-ethoxycarbonyl-1-butyl]-L-alanine with 4-(4,6-dimethoxy-1,3,5-triazin-2-yl)-4-methylmorpholinium chloride in a solvent and its use in the synthesis of perindopril, perindopril erbumine or pharmaceutically acceptable salts by reaction of I with compound (II) (R1 = aryl, alkyl, or silyl protective group) in a solvent, following by deprotection of compound (III) using suitable deprotecting agent, is described. Thus, N-[1-(S)-ethoxycarbonyl-1-butyl]-L-alanine and 4-(4,6-dimethoxy-1,3,5-triazin-2-yl)-4-methylmorpholinium chloride were mixed in THF and stirred for about 10 min at t° = 20-25° under nitrogen. To the resulting solution contained complex I was added (2S, 3aS, 7aS)-benzyl-perhydroindole-2-carboxylate at t° = 20-25° under nitrogen, and after separation and purification 1.5 g of perindopril benzyl ester was obtained, which was transformed into perindopril tert-Bu amine salt.

RX(1) OF 3   A + B ===> C...



RX(1)   RCT A 82834-12-6

    STAGE(1)
        RGT D 3945-69-5 Morpholinium,
            4-(4,6-dimethoxy-1,3,5-triazin-2-yl)-4-methyl-, chloride
            (1:1)
        SOL 109-99-9 THF
        CON 10 minutes, 20 - 25 deg C

    STAGE(2)
        RCT B 83508-14-9
        CON 5 - 6 hours, 20 - 25 deg C

    PRO C 122454-52-8

L2 ANSWER 4 OF 15 CASREACT COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 146:184735 CASREACT Full-text

TITLE: Process for manufacture of (2S,3aS,7aS)-1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-1H-indole-2-carboxylic acid (perindopril) and its tert-butyl amine salt

INVENTOR(S): Gunjal, Sanjay Tukaram; Jadhav, Dilip Uttam; Kumar, Ashok; Arpana, Mathur; Panda, Nalinakshya Balaram; Soudagar, Satish Rajanikant

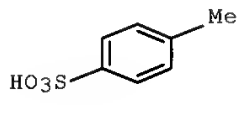
PATENT ASSIGNEE(S): India
SOURCE: U.S. Pat. Appl. Publ., 10 pp., Cont.-in-part of U.S. Ser. No. 140,226.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20070021490	A1	20070125	US 2006-324349	20060103
IN 2005MU00017	A	20060811	IN 2005-MU17	20050106
US 20060178422	A1	20060810	US 2005-140226	20050527
PRIORITY APPLN. INFO.:			IN 2005-MU17	20050106
			US 2005-140226	20050527
			IN 2004-MU566	20040518

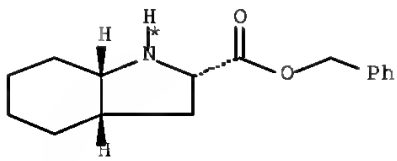
OTHER SOURCE(S): MARPAT 146:184735

AB The invention relates to the preparation of perindopril [(2S,3aS,7aS)-1-[(2S)-2-[(S)-1-(ethoxycarbonyl)butylamino]propionyl]octahydro-1H-indole-2-carboxylic acid], its salts, and its novel intermediates, specifically aralkyl ester salts. Thus, (2S,3aS,7aS)-octahydro-1H-indole-2-carboxylic acid was treated with N-[(S)-1-(ethoxycarbonyl)butyl]-L-alanine in CH2Cl2 in the presence of Et3N, 1-hydroxybenzotriazole, and dicyclohexylcarbodiimide to afford 99% perindopril benzyl ester. Conversion of the latter into the oxalate salt, followed by hydrogenolysis over 5% Pd/C and reaction with tert-butylamine yielded perindopril erbumine.

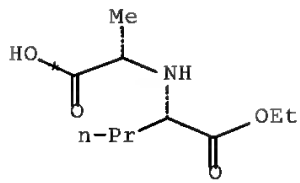
RX(1) OF 38 A + B ===> C...



A: CM 1



A: CM 2



B

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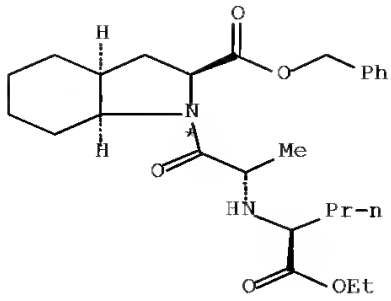


C
YIELD 99%

RX(1) RCT A 94062-52-9

STAGE(1)
RGT D 121-44-8 Et3N
SOL 75-09-2 CH2Cl2
CON 20 - 25 deg C

STAGE(2)
RCT B 82834-12-6
RGT E 2592-95-2 1-Benzotriazolol, F 538-75-0 DCC
CON SUBSTAGE(1) 15 minutes, 20 - 25 deg C
SUBSTAGE(2) 20 - 25 deg C

PRO C 122454-52-8

L2 ANSWER 5 OF 15 CASREACT COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 146:45750 CASREACT Full-text
TITLE: Process for the preparation of perindopril
INVENTOR(S): Sinha, Brajesh Kumar; Vaddi, Pandu Ranga Rao; Budidet, Shankar Reddy; Dandala, Ramesh; Meenakshisunderam, Sivakumaran
PATENT ASSIGNEE(S): Aurobindo Pharma Limited, India
SOURCE: PCT Int. Appl., 16pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006131828	A1	20061214	WO 2006-IB1583	20060601

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,

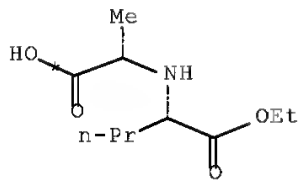
CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

IN 2005CH00703	A	20070727	IN 2005-CH703	20050608
IN 2005CH01355	A	20070928	IN 2005-CH1355	20050926
PRIORITY APPLN. INFO.:			IN 2005-CH703	20050608
			IN 2005-CH1355	20050926

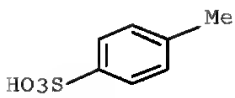
OTHER SOURCE(S): MARPAT 146:45750

AB An improved process for the preparation of perindopril [(2S,3aS,7aS)-1-[(2S)-2-[(S)-1-(ethoxycarbonyl)butylamino]propionyl]octahydro-1H-indole-2-carboxylic acid] comprises treating (2S,3aS,7aS)-octahydro-1H-indole-2-carboxylic acid benzyl ester p-toluenesulfonic acid salt with N-[(S)-1-(ethoxycarbonyl)butyl]-L-alanine [e.g., in MeCN in the presence of 4-(dimethylamino)pyridine], followed by hydrogenolysis of perindopril benzyl ester over 5% Pd/C.

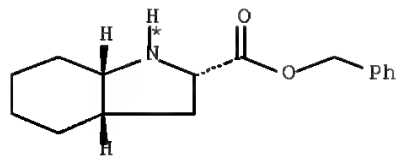
RX(2) OF 4 A + B ===> I...



A

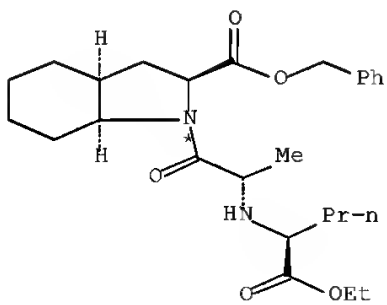


B: CM 1



B: CM 2

(2) →



I

RX(2) RCT A 82834-12-6

STAGE(1)
RGT D 7693-46-1 ClCO2C6H4NO2-4, J 121-44-8 Et3N
SOL 141-78-6 AcOEt
CON SUBSTAGE(1) 0 - 10 deg C
SUBSTAGE(2) 10 deg C -> 20 deg C
SUBSTAGE(3) 1 hour, 20 - 25 deg C

STAGE(2)
RGT K 2592-95-2 1-Benzotriazolol
CON SUBSTAGE(1) 20 - 25 deg C
SUBSTAGE(2) 10 minutes, 20 - 25 deg C

STAGE(3)
RCT B 94062-52-9
RGT J 121-44-8 Et3N
CON SUBSTAGE(2) 20 - 30 deg C

STAGE(4)
RGT E 1122-58-3 4-DMAP
CON SUBSTAGE(2) 3 hours, 30 - 35 deg C

PRO I 122454-52-8
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

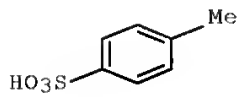
L2 ANSWER 6 OF 15 CASREACT COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 145:230528 CASREACT Full-text
TITLE: Process for making highly pure perindopril erbumine
INVENTOR(S): Kumar, Ashok; Soudagar, Satish Rajanikant; Mathur, Arpana; Shah, Chirag Hasmukh; Gunjal, Sanjay Tukaram; Metil, Dattatray Shamrao; Kelkar, Rahul Suresh; Thakare, Devendra Digambar; Kumar, Bindu Manoj; Nair, Raji
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 6 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20060178422	A1	20060810	US 2005-140226	20050527
IN 2004MU00566	A	20060616	IN 2004-MU566	20040518
US 20070021490	A1	20070125	US 2006-324349	20060103
PRIORITY APPLN. INFO.:			IN 2004-MU566	20040518
			IN 2005-MU17	20050106
			US 2005-140226	20050527

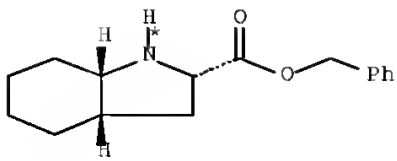
AB A process for the synthesis and isolation of (2S,3aS,7aS)-1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1- oxopropyl]octahydro-1H-indole-2-carboxylic acid and its tert-butylamine salt, comprises the amidation of (2S,3aS,7aS)-octahydroindole-2-carboxylic acid benzyl ester and N-[(S)1-carboxybutyl]-(S)-alanine Et ester in nonreactive solvents in turn avoiding the formation of the impurity N-acetyl (2S,3aS,7aS)-octahydroindole-2-carboxylic acid benzyl ester. The de-protection of benzyl ester group is optimized by catalytic

hydrogenolysis and then isolation of the product from an aqueous layer by extraction using an organic solvent, which eliminates the need for lyophilization. This yields perindopril erbumine free of contaminants derivable from dicyclohexylcarbodiimide (e.g., dicyclohexylurea) and impurities originated by the use of Et acetate.

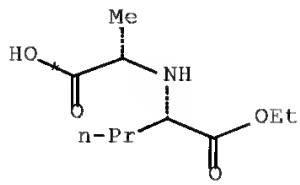
RX(1) OF 3 A + B ===> C...



A: CM 1

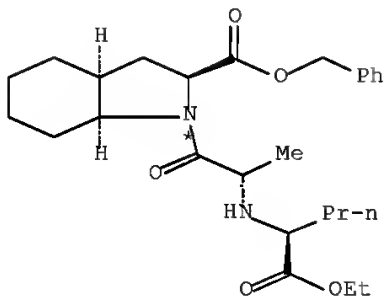


A: CM 2



B

(1)
→



C
YIELD 99%

RX(1) RCT A 94062-52-9, B 82834-12-6
RGT D 538-75-0 DCC, E 121-44-8 Et3N
PRO C 122454-52-8
SOL 75-09-2 CH2Cl2
CON SUBSTAGE(1) 0.25 hours, room temperature
SUBSTAGE(2) 20 - 25 deg C

L2 ANSWER 7 OF 15 CASREACT COPYRIGHT 2009 ACS on STN

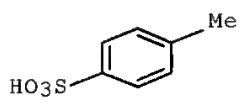
ACCESSION NUMBER: 145:124844 CASREACT Full-text
TITLE: Process for the synthesis of (2S,3aS,7aS)-1-(S)-alanyloctahydro-1H-indole-2-carboxylic acid derivatives and use in the synthesis of perindopril
INVENTOR(S): Kumar, Ashok; Soudagar, Satish Rajanikant; Mathur, Arpana; Gunjal, Sanjay Tukaram; Panda, Nalinakshya Balaram; Jadhav, Dilip Uttam
PATENT ASSIGNEE(S): IPCA Laboratories Limited, India
SOURCE: Eur. Pat. Appl., 16 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1679072	A1	20060712	EP 2005-113099	20051230
EP 1679072	B1	20080924		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, BA, HR, IS, YU				
IN 2005MU00017	A	20060811	IN 2005-MU17	20050106
AT 409036	T	20081015	AT 2005-113099	20051230
EP 1987828	A1	20081105	EP 2008-104990	20051230
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR				

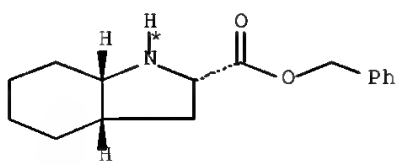
PRIORITY APPLN. INFO.: IN 2005-MU17 20050106
EP 2005-113099 20051230

AB The invention relates perindopril [(2S,3aS,7aS)-1-[(2S)-2-[(S)-1-(ethoxycarbonyl)butylamino]propionyl]octahydro-1H-indole-2-carboxylic acid] aralkyl ester salts used in the synthesis of perindopril. Thus, (2S,3aS,7aS)-octahydro-1H-indole-2-carboxylic acid was treated with N-[(S)-1-(ethoxycarbonyl)butyl]-L-alanine in CH2Cl2 in the presence of Et3N, 1-hydroxybenzotriazole, and dicyclohexylcarbodiimide to afford 99% perindopril benzyl ester. Conversion of the latter into the oxalate salt, followed by hydrogenolysis over 5% Pd/C and reaction with tert-butylamine yielded perindopril erbumine.

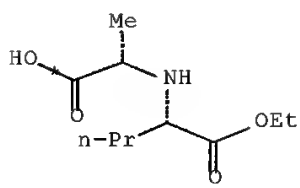
RX(1) OF 34 A + B ===> C...



A: CM 1



A: CM 2



B

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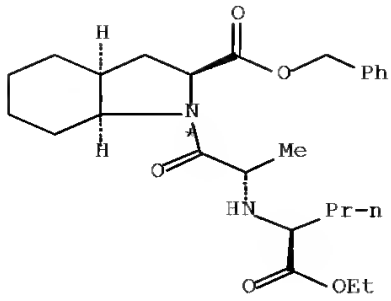
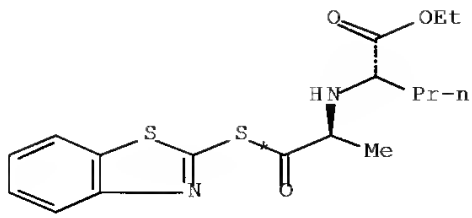


C
YIELD 99%

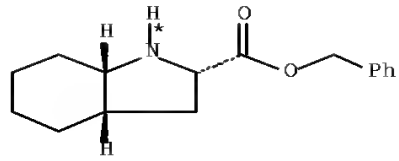
RX(1) RCT A 94062-52-9, B 82834-12-6
RGT D 121-44-8 Et3N, E 2592-95-2 1-Benzotriazolol
PRO C 122454-52-8
SOL 75-09-2 CH2Cl2
CON SUBSTAGE(1) 20 - 25 deg C
SUBSTAGE(2) 0.25 hours, 20 - 25 deg C
SUBSTAGE(3) 20 - 25 deg C
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 8 OF 15 CASREACT COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 142:430514 CASREACT Full-text
TITLE: 2'-Benzothiazolylthioesters of N-substituted alpha amino acids: versatile intermediates for synthesis of ACE inhibitors
AUTHOR(S): Singh, Girij Pal; Godbole, Himanshu M.; Nehate, Sagar P.; Mahajan, Pravin R.
CORPORATE SOURCE: Lupin Research Park, Lupin Ltd., Pune, India
SOURCE: Synthetic Communications (2005), 35(2), 243-248
CODEN: SYNCAV; ISSN: 0039-7911
PUBLISHER: Taylor & Francis, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB ACE (angiotensin-converting enzyme) inhibitors have been synthesized in high diastereomeric selectivity by condensation of novel activated amino esters with cyclic amino acid esters using simple reaction conditions. The activated amino esters may be obtained from the corresponding carboxylic acids or their acid chlorides by activation with 2-mercapto-benzothiazole.

RX(5) OF 19 ...C + O ===> P...

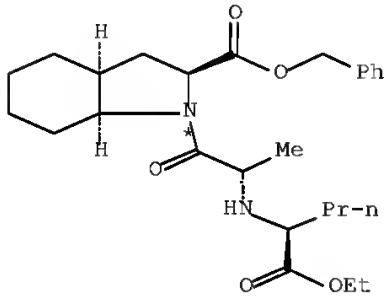


C



O

(5)



P
YIELD 80%

RX(5) RCT C 827622-31-1, O 83508-14-9

STAGE(1)
RGT M 121-44-8 Et3N
SOL 75-09-2 CH2Cl2
CON 4 hours, -15 - -10 deg C

STAGE(2)
RGT Q 1310-73-2 NaOH
SOL 7732-18-5 Water
CON 2 hours, pH 8.3 - 8.6

PRO P 122454-52-8
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 9 OF 15 CASREACT COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 142:156329 CASREACT Full-text
TITLE: Preparation of α-amino acid benzothiazolylthio

esters as intermediates for manufacture of ACE inhibitors

INVENTOR(S): Singh, Girij Pal; Godbole, Himanshu Madhav; Mahajan, Pravin Raghunath; Nehate, Sagar Purushottam

PATENT ASSIGNEE(S): Lupin Limited, India

SOURCE: PCT Int. Appl., 108 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

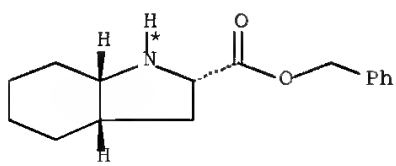
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005010028	A1	20050203	WO 2003-IN257	20030731
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003272077	A1	20050214	AU 2003-272077	20030731

PRIORITY APPLN. INFO.: WO 2003-IN257 20030731

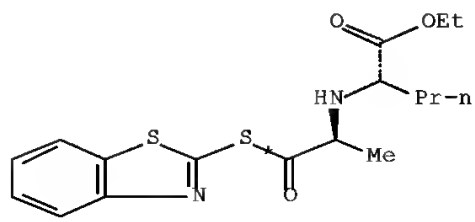
OTHER SOURCE(S): MARPAT 142:156329

AB The invention relates to esters (S,S)-RCH2CH2CH(CO2R1)NHCHR2CO-X (I; R is alkyl or Ph; R1 H or alkyl; R2 is alkyl or aminoalkyl; X is 2-benzothiazolylthio) which are intermediates in the manufacture of ACE inhibitors I (X is an amino acid or derivative). The intermediate benzothiazolylthio esters were prepared by reaction of the appropriate acid or acid chloride with 2,2'-dithiobis(benzthiazole) or 2-mercaptobenzothiazole. Thus, treatment of N-[1(S)-(ethoxycarbonyl)-3-phenylpropyl]-N6-(trifluoroacetyl)-L-lysine (preparation given) with 2,2'-dithiobis(benzothiazole), followed by coupling with L-proline Et ester and deprotection, afforded lisinopril dihydrate.

RX(6) OF 48 ...R + C ===> S...

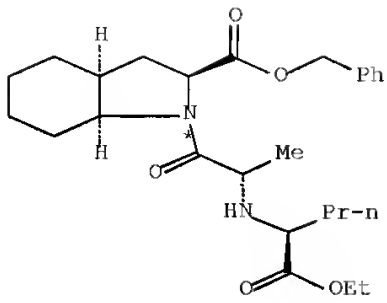


R



C

(6) →



S
YIELD 80%

RX(6) RCT R 83508-14-9

STAGE(1)
RGT E 121-44-8 Et3N
SOL 75-09-2 CH2C12
CON SUBSTAGE(1) 25 - 30 deg C
SUBSTAGE(2) 30 deg C -> 15 deg C

STAGE(2)
RCT C 827622-31-1
CON SUBSTAGE(1) 1 hour
SUBSTAGE(2) 25 - 30 deg C
SUBSTAGE(3) 8 - 10 hours

STAGE(3)
RGT T 7732-18-5 Water

PRO S 122454-52-8
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 10 OF 15 CASREACT COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 141:411226 CASREACT Full-text
TITLE: Process for preparation of perindopril and its salts
INVENTOR(S): Kankan, Rajendra Narayanrao; Rao, Dharmaraj Ramachandra
PATENT ASSIGNEE(S): Cipla Limited, India; Wain, Christopher Paul
SOURCE: PCT Int. Appl., 26 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004099138	A2	20041118	WO 2004-GB2029	20040512
WO 2004099138	A3	20041223		

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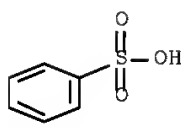
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

IN 2003MU00468	A	20050211	IN 2003-MU468	20030512
PRIORITY APPLN. INFO.:			IN 2003-MU468	20030512

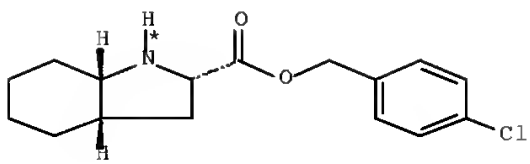
OTHER SOURCE(S): MARPAT 141:411226

AB A process for preparing perindopril or a pharmaceutically-acceptable salt comprises esterifying (2S,3aS,7aS)-octahydro-1H-indole-2-carboxylic acid (I) with benzyl alc. (or the 4-chloro or 4-alkoxy derivative) in the presence of benzenesulfonic acid as catalyst, treating the intermediate ester benzenesulfonate with N-[(S)-1-carbethoxybutyl]-L-alanine (II), and ester cleavage. Thus, I benzyl ester benzenesulfonate (40 g) was prepared, its suspension in CH2Cl2 made alkaline with aqueous ammonia, and the organic layer separated Treatment with II at 10-15 °C in the presence of hydroxybenzotriazole and N,N'-dicyclohexylcarbodiimide and workup afforded 43 g perindopril benzyl ester.

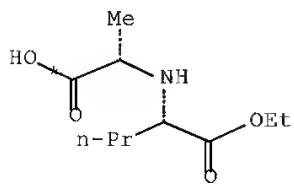
RX(3) OF 10 G + H ===> I...



G: CM 1

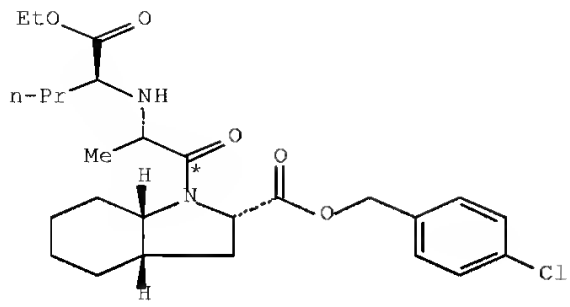


G: CM 2



H

(3) ⟶



I

RX(3) RCT G 793716-55-9

STAGE(1)
RGT J 7664-41-7 NH3
SOL 7732-18-5 Water, 75-09-2 CH2Cl2
CON SUBSTAGE(1) room temperature
SUBSTAGE(2) room temperature
SUBSTAGE(3) 0.5 hours, room temperature

STAGE(2)
RCT H 82834-12-6
RGT K 2592-95-2 1-Benzotriazolol, L 538-75-0 DCC
SOL 75-09-2 CH2Cl2
CON SUBSTAGE(1) 10 - 15 deg C
SUBSTAGE(2) 10 - 15 deg C

PRO I 793716-56-0
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 11 OF 15 CASREACT COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 141:395815 CASREACT Full-text
TITLE: A process for the preparation of perindopril using tetramethyluronium salts as coupling reagents
INVENTOR(S): Rucman, Rudolf
PATENT ASSIGNEE(S): Lek Pharmaceuticals D.D., Slovenia
SOURCE: PCT Int. Appl., 15 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004099236	A1	20041118	WO 2004-SI20	20040507

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,

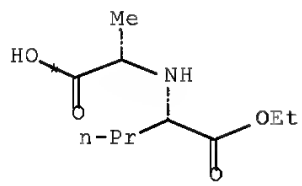
GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
SN, TD, TG

SI 21506	A	20041231	SI 2003-118	20030508
EP 1628995	A1	20060301	EP 2004-731809	20040507
EP 1628995	B1	20070627		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
AT 365745	T	20070715	AT 2004-731809	20040507
ES 2287725	T3	20071216	ES 2004-731809	20040507
US 20070173637	A1	20070726	US 2006-555848	20061026
PRIORITY APPLN. INFO.:			SI 2003-118	20030508
			WO 2004-SI20	20040507

OTHER SOURCE(S): MARPAT 141:395815

AB A process for the preparation of the ACE inhibitor perindopril involves activation of N-[1(S)-(ethoxycarbonyl)butyl]-(S)-alanine (1) with a tetramethyluronium salt in the presence of a tertiary organic base, coupling with (2S,3aS,7aS)-octahydroindole-2-carboxylic acid (2) or an ester, and deprotection. Thus, a mixture of 1, 2 benzyl ester, TBTU and diisopropylethylamine in DMF/CH2Cl2 was stirred for 4 h to afford benzyl-perindopril, which was converted to perindopril by phase transfer or classical hydrogenation.

RX(2) OF 4 F + G ===> A...



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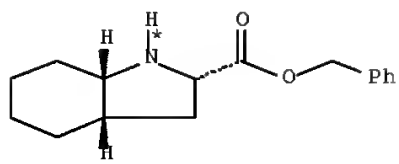

G

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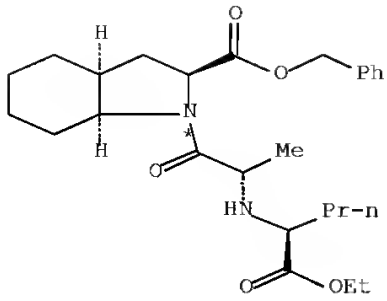


A
YIELD 98%

RX(2) RCT F 82834-12-6

STAGE(1)
RGT H 125700-67-6 Benzotriazolium der, I 7087-68-5 EtN(Pr-i)2
SOL 75-09-2 CH2C12, 68-12-2 DMF
CON SUBSTAGE(1) room temperature
SUBSTAGE(2) 10 minutes, room temperature

STAGE(2)
RCT G 83508-14-9
SOL 75-09-2 CH2C12
CON SUBSTAGE(1) room temperature
SUBSTAGE(2) 4 hours, room temperature

PRO A 122454-52-8
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 12 OF 15 CASREACT COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 141:243833 CASREACT Full-text
TITLE: Process for preparation of perindopril and its salts
INVENTOR(S): Datta, Debashish; Singh, Girij Pal; Godbole, Himanshu Madhav; Siyan, Rajinder Singh
PATENT ASSIGNEE(S): Lupin Limited, India
SOURCE: PCT Int. Appl., 46 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004075889	A1	20040910	WO 2003-IN42	20030228

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,

KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF,
BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2517205	A1	20040910	CA 2003-2517205	20030228
AU 2003224420	A1	20040917	AU 2003-224420	20030228
EP 1603558	A1	20051214	EP 2003-720846	20030228
EP 1603558	B1	20080521		

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK

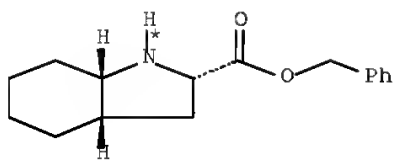
JP 2006519168	T	20060824	JP 2004-568714	20030228
AT 395913	T	20080615	AT 2003-720846	20030228
ES 2307923	T3	20081201	ES 2003-720846	20030228
US 20060276659	A1	20061207	US 2006-547243	20060621

PRIORITY APPLN. INFO.: WO 2003-IN42 20030228

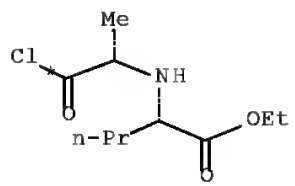
OTHER SOURCE(S): MARPAT 141:243833

AB A process for the preparation of perindopril and its salts involves reaction of N-[1(S)-(ethoxycarbonyl)butyl]-L-alanyl chloride (I) or bromide with (2S)-indolinecarboxylic acid benzyl ester or its hexahydro derivative, followed by catalytic hydrogenation. Thus, perindopril benzyl ester was prepared by adding a slurry of 1.88 g I (preparation given) to a solution of 1.6 g (2S,3aS,7aS)-octahydroindole-2-carboxylic acid benzyl ester and triethylamine in CH2Cl2 at -10 to 15° over 25-30 min. Hydrogenation of the benzyl ester over 10% Pd-C afforded 1.3 g perindopril.

RX(6) OF 28 ...T + B ===> F...

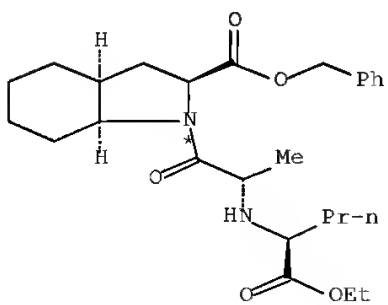


T



B

(6)



F

RX(6) RCT T 83508-14-9, B 748154-69-0

STAGE(1)
RGT U 121-44-8 Et3N
SOL 75-09-2 CH2C12
CON SUBSTAGE(1) 25 - 30 minutes
SUBSTAGE(2) 25 - 30 deg C

STAGE(2)
RGT N 7732-18-5 Water

PRO F 122454-52-8
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

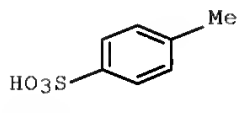
L2 ANSWER 13 OF 15 CASREACT COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 140:375491 CASREACT Full-text
TITLE: Method for the synthesis of perindopril and its pharmaceutically-acceptable salts
INVENTOR(S): Dubuffet, Thierry; Lecouve, Jean-Pierre
PATENT ASSIGNEE(S): Les Laboratoires Servier, Fr.
SOURCE: Eur. Pat. Appl., 6 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1420029	A2	20040519	EP 2003-293084	20031210
EP 1420029	A3	20040526		
EP 1420029	B1	20080220		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
AT 386745	T	20080315	AT 2003-293084	20031210
ES 2300555	T3	20080616	ES 2003-293084	20031210
AU 2004312185	A1	20050721	AU 2004-312185	20041209
CA 2548405	A1	20050721	CA 2004-2548405	20041209
WO 2005066198	A1	20050721	WO 2004-FR3166	20041209
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CN 1890258	A	20070103	CN 2004-80036354	20041209
BR 2004017423	A	20070306	BR 2004-17423	20041209
JP 2008505845	T	20080228	JP 2006-543583	20041209
IN 2006DN03069	A	20070824	IN 2006-DN3069	20060529
MX 2006006562	A	20060731	MX 2006-6562	20060609
US 20070093663	A1	20070426	US 2006-582283	20060609
US 7279583	B2	20071009		

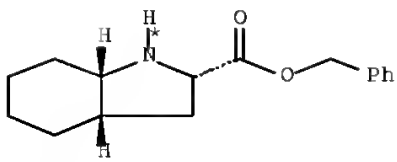
NO 2006003012	A	20060628	NO 2006-3012	20060628
KR 825537	B1	20080425	KR 2006-713586	20060706
PRIORITY APPLN. INFO.:			EP 2003-293084	20031210
			WO 2004-FR3166	20041209

AB A method for the synthesis of perindopril involves coupling of (2S)-indoline-2-carboxylic acid benzyl ester or (2S,3aS,7aS)-octahydroindole-2-carboxylic acid benzyl ester with N-[(S)-1-carbethoxybutyl]-L-alanine in the presence of a coupling agent [e.g., O-(benzotriazol-1-yl)-1,1,3,3-bis(tetramethylene)uronium hexafluorophosphate], followed by hydrogenation over Pd. Perindopril was converted into its tert-butylamine salt.

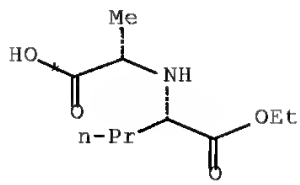
RX(1) OF 4 A + B ===> C...



A: CM 1

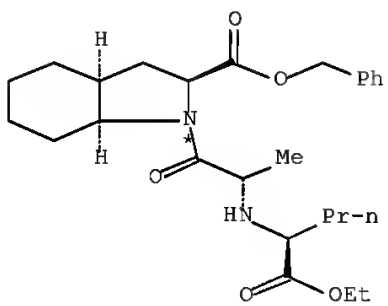


A: CM 2



B

(1)



C

RX(1) RCT A 94062-52-9

STAGE(1)
RGT D 121-44-8 Et3N
SOL 141-78-6 AcOEt

```
            CON  10 minutes, room temperature

          STAGE(2)
            RCT  B 82834-12-6
            RGT  E 105379-24-6 1H-Benzotriazolium,
                 1-(di-1-pyrrolidinylmethylene)-, 3-oxide,
                 hexafluorophosphate(1-) (1:1)
            CON  SUBSTAGE(1) room temperature -> 30 deg C
                 SUBSTAGE(2) 3 hours, 30 deg C

       PRO  C 122454-52-8
REFERENCE COUNT:          1     THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS
                                RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT


L2   ANSWER 14 OF 15  CASREACT  COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER:        135:167034  CASREACT  Full-text
TITLE:                   Method for synthesis of perindopril and its
                         pharmaceutically acceptable salts
INVENTOR(S):             Langlois, Pascal; Turbe, Hugues
PATENT ASSIGNEE(S):      Adir et Compagnie, Fr.
SOURCE:                  PCT Int. Appl., 18 pp.
                         CODEN: PIXXD2
DOCUMENT TYPE:           Patent
LANGUAGE:                French
FAMILY ACC. NUM. COUNT:  1
PATENT INFORMATION:

     PATENT NO.        KIND  DATE           APPLICATION NO.  DATE
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     WO 2001058868      A1   20010816       WO 2001-FR1026   20010405
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
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             HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS,
             LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO,
             RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ,
             VN, YU, ZA, ZW
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
             DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
             BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
     FR 2807431         A1   20011012       FR 2000-4379     20000406
     FR 2807431         B1   20020719
     HU 2001001336      A2   20020228       HU 2001-1336     20010330
     HU 2001001336      A3   20030328
     CA 2405486         A1   20010816       CA 2001-2405486  20010405
     CA 2405486         C    20080729
     AU 2001048470      A    20010820       AU 2001-48470    20010405
     EP 1268424         A1   20030102       EP 2001-921486   20010405
     EP 1268424         B1   20070808
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
     BR 2001009836      A    20030624       BR 2001-9836     20010405
     JP 2003531825      T    20031028       JP 2001-558419   20010405
     JP 3939553         B2   20070704
     NZ 521454          A    20040326       NZ 2001-521454   20010405
     EE 200200575       A    20040415       EE 2002-575      20010405
     EE 5032            B1   20080616
     AU 2001248470      B2   20050120       AU 2001-248470   20010405
     AP 1385            A    20050408       AP 2002-2630     20010405
     CN 1296355         C    20070124       CN 2001-807372   20010405
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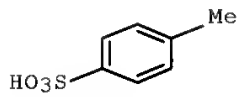
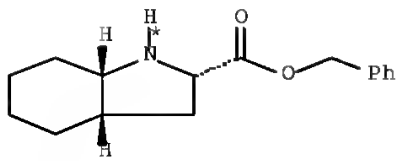
AT 369338	T	20070815	AT 2001-921486	20010405
ES 2291307	T3	20080301	ES 2001-921486	20010405
IN 2002MU00598	A	20040417	IN 2002-MU598	20020703
ZA 2002007419	A	20030916	ZA 2002-7419	20020916
IN 2002MN01284	A	20040703	IN 2002-MN1284	20020918
US 20030069431	A1	20030410	US 2002-239129	20020919
US 6835843	B2	20041228		
MX 2002009706	A	20040906	MX 2002-9706	20021002
NO 2002004808	A	20021004	NO 2002-4808	20021004
NO 324174	B1	20070903		
BG 107249	A	20030731	BG 2002-107249	20021104
HK 1053309	A1	20070511	HK 2003-105542	20030801
PRIORITY APPLN. INFO.:			FR 2000-4379	20000406
			WO 2001-FR1026	20010405

AB Perindopril [(2S,3aS,7aS)-1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butylamino]propionyl]octahydro-1H-indole-2-carboxylic acid] was prepared by coupling (2S,3aS,7aS)octahydroindole-2-carboxylic acid tosylate with N-[(S)-1-carbethoxybutyl]-(S)-alanine, followed by catalytic hydrogenation to remove the benzyl group. In an example, the coupling reaction was carried out in Et acetate in the presence of Et3N, 1-hydroxybenzotriazole and dicyclohexylcarbodiimide at 30° for 3h to give 92% perindopril benzyl ester.

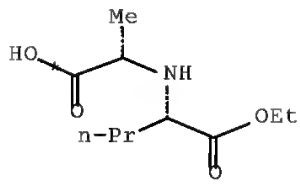
RX(1) OF 3 A + B ===> C...



A: CM 1

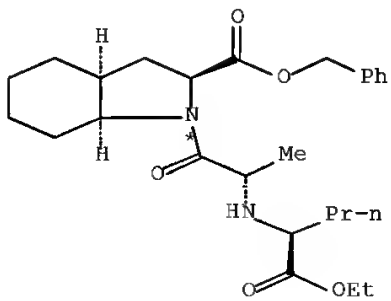


A: CM 2



B

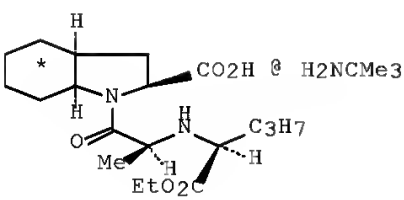
(1) →



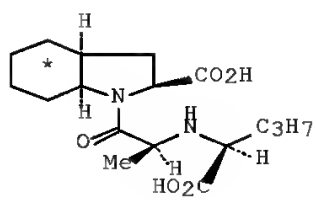
C
YIELD 92%

RX(1) RCT A 94062-52-9, B 82834-12-6
RGT D 121-44-8 Et3N, E 2592-95-2 1-Benzotriazolol, F 538-75-0 DCC
PRO C 122454-52-8
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 15 OF 15 CASREACT COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 109:231529 CASREACT Full-text
TITLE: Synthesis of S9490-3 [U-14C-cyclohexyl] 1-[(2S)2-[(1S)1-(ethoxycarbonylbutyl)amino]-1-oxopropyl]-(2S,3aS,7aS)-perhydroindole-2-carboxylic acid tert-butylamine salt and S9780 [U-14C-cyclohexyl] 1-[(2S)2-[(1S)1-(carboxybutyl)amino]-1-oxopropyl]-2S,3aS,7aS)-perhydroindole-2-carboxylic acid and of [3,4-3H-butylamino]S9490-3 and [(3,4-3H-)butylamino]S9780
AUTHOR(S): Pichat, L.; Tostain, J.; Gomis, J. M.; Coppo, M.; Moustier, A. M.; Vincent, M.; Remond, G.; Portevin, B.; Laubie, M.
CORPORATE SOURCE: CEN Saclay, Gif sur Yvette, 91191, Fr.
SOURCE: Journal of Labelled Compounds and Radiopharmaceuticals (1988), 25(5), 553-68
CODEN: JLCRD4; ISSN: 0362-4803
DOCUMENT TYPE: Journal
LANGUAGE: French
GI



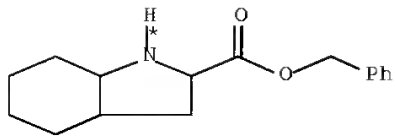
I



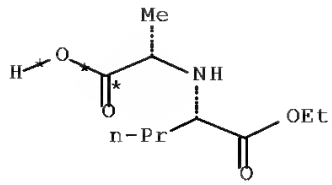
II

AB The title 14C-labeled compds. I (* signifies the uniform labeling of the cyclohexane ring with 14C) and II were prepared from aniline-U-14C in several steps. The title 3H-labeled compds. were also prepared The latter synthesis involved the tritiation of an allylglycine residue. The title compds. are potent inhibitors of angiotensin-converting enzyme.

RX(10) OF 69 ...Y + AB ===> A...

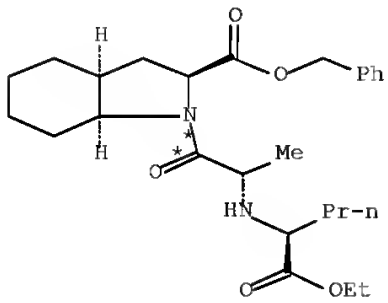


Y



AB

(10)



A

RX(10) RCT Y 117770-56-6, AB 82834-12-6
RGT AC 538-75-0 DCC, AD 2592-95-2 1-Benzotriazolol
PRO A 117770-57-7
SOL 68-12-2 DMF

=> log off
ALL L# QUERIES AND ANSWER SETS ARE DELETED AT LOGOFF
LOGOFF? (Y)/N/HOLD:y
STN INTERNATIONAL LOGOFF AT 12:58:34 ON 06 MAR 2009